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Effect of Toxaphene on Pyruvic and Lactic Acid Levels in the Rat

by David B. Peakall*

Rats were given a single dose of toxaphene (120 mg/kg equivalent to $^1/_2$ LD_{50}) and sacrificed at 1, 5, and 15 days. No alterations of levels of pyruvic or lactic acid in blood plasma were observed. In a second experiment, rats were given 2.4 mg/kg daily and sacrificed at 1, 3, and 6 months, and again no alterations of pyruvic or lactic acid levels were found. It is concluded that observed alterations of the activity of lactic acid dehydrogenase induced by toxaphene do not give rise to physiological changes in unstressed rats.

Introduction

Recent studies (*1*, *2*) have shown that the activity of the enzyme lactate dehydrogenase (LDH) is decreased in the blood serum, liver, and kidneys of rats exposed to toxaphene. In this paper the physiological consequences of these alterations are examined by determining the levels of pyruvic and lactic acids in the serum of rats exposed to the same regime of toxaphene as used by Kuz'minskaya and Alekhina (*1*).

Materials and Methods

The experiments were divided into two sections, short-term and chronic administration. In the short-term experiments, male rats were given toxaphene orally by capsule as a single dose of $^1/_2$ LD_{50} (120 mg/kg), and animals sacrificed at 1, 5, and 15 days. In the chronic experiments the animals were fed 1/100 LD_{50} daily for 1, 3, and 6 months. At sacrifice, blood samples were taken and the liver removed for analysis. Levels of lactate and pyruvate were measured spectrophotometrically in deproteinized blood by the method of Olsen (*3*). Levels of toxaphene in the liver were determined by gas-liquid chromatography by using the method of Wilson (*4*).

* Wildlife Toxicology Division, Canadian Wildlife Service, Ottawa, Ontario, Canada, K1A OH3.

Results

The basic results of the experiments are given in Table 1. No significant alteration of either pyruvic or lactic acids were found either in the short-term single dose experiments nor in the chronic, daily dose animals. The levels found in blood are similar to those reported to other workers (*5*, *6*). The residue data indicated that equilibrium in the liver had been reached within one month on dosage and that equilibrium levels in the brain were reached within one to three months.

Discussion

The work of Gertig and Nowaczyk (*2*) and that of Kuz'minskaya and Alekhina (*1*) showed that toxaphene does alter the activity of the enzyme lactic dehydrogenase. The results presented here indicate that this alteration is not enough to have definite physiological consequences under the conditions of the experiment. The major importance of lactic acid is in its conversion to glycogen when the animal is in oxygen debt following exertion. This process is outlined in Figure 1. A criticism of the current study is that it was not carried out under the stress of exercise. The pyruvate-lactate shunt (see Fig. 2) is more important under conditions of excessive exercise and presumably under these conditions the capacity of the enzyme system would be more fully extended. Under normal conditions, it appears that either there is enough reserve capacity in the enzyme system of the pyruvate-lactate shunt, or that

Table 1. Effect of toxaphene on blood plasma levels of lactic and pyruvic acids.

Time on toxaphene[a]	Level of toxaphene, ppm wet weight[b]		Blood plasma levels, mg/100 ml[b]	
	Liver	Brain	Lactic acid	Pyruvic acid
1 day	2.3 ± 0.4 (4)	Not detected	7.7 ± 0.6 (6)	2.0 ± 0.2 (6)
5 days	4.2 ± 1.8 (4)	2.0 ± 1.0 (4)	7.5 ± 0.6 (6)	1.8 ± 0.2 (6)
15 days	5.7 ± 2.3 (4)	2.7 ± 1.4 (4)	8.1 ± 0.6 (6)	2.1 ± 0.3 (6)
1 month	27.7 ± 2.3 (4)	9.3 ± 1.1 (4)	7.3 ± 0.7 (6)	2.2 ± 0.3 (6)
3 months	26.4 ± 1.7 (4)	12.7 ± 1.5 (4)	7.5 ± 0.6 (6)	1.9 ± 0.2 (6)
6 months	25.7 ± 2.1 (4)	12.0 ± 1.3 (4)	8.2 ± 0.8 (6)	2.1 ± 0.3 (6)

[a] 1-15 day animals were exposed to a single dose of 120 mg/kg; 1-6 month animals were given 2.4 mg/kg daily.
[b] Mean, standard deviation, and sample size.

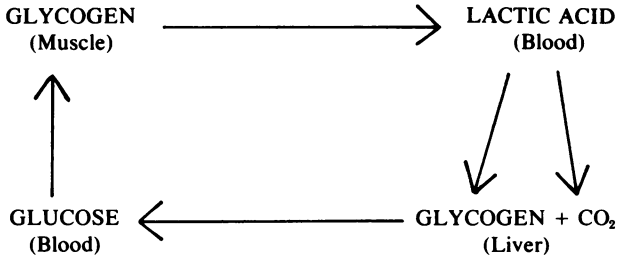

FIGURE 1. Overall utilization of lactic acid during exercise.

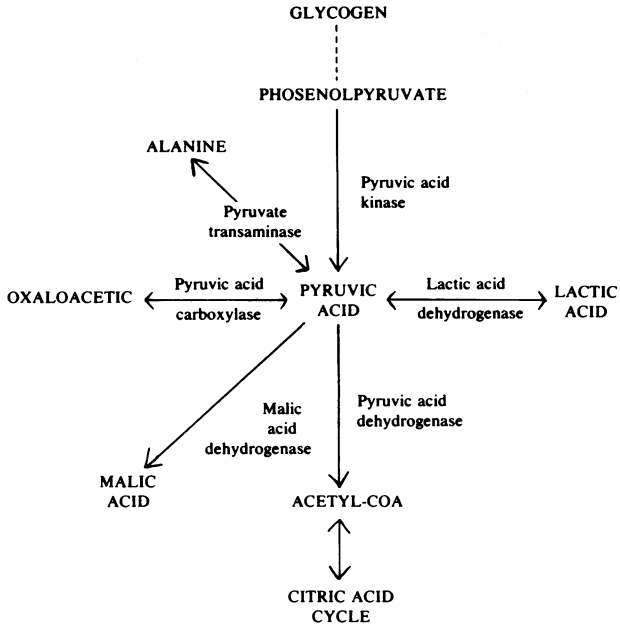

FIGURE 2. Metabolic pathways involving pyruvic and lactic acids.

with a complex, interrelated system (Fig. 2) alterations in one part of the system can be compensated for by alterations in other pathways.

Bhatia et al. (5) found that a single sublethal dose of dieldrin (30 mg/kg, CV, equivalent to 65% of LD_{50}) caused significant increase of the levels of pyruvic and lactic acids 20–24 hr after injection. These authors consider that these changes could be due to inhibition of pyruvate oxidation or to increase demand due to the stimulation of hepatic glucose. In contrast, the results given here show that a single, sublethal dose of toxaphene does not act similarly to dieldrin.

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